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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FERNANDEZ, SUSAN EMILY	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 09/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/919,102	FEIN, HOWARD	
	Examiner	Art Unit	
	Susan E. Fernandez	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,5,8,9,24,25,30,31,34,35,37-40 and 43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,5,8,9,24,25,30,31,34,35,37-40 and 43* is/are rejected.

7)☒ Claim(s) *1,24,30 and 34* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 7, 2006, has been entered.

Claims 3, 6, 7, 10-23, 26-29, 32, 33, 36, 41, 42, and 44-63 are canceled.

Claims 1, 2, 4, 5, 8, 9, 24, 25, 30, 31, 34, 35, 37-40, and 43 are pending and are examined on the merits to the extent they read on the elected subject matter and species (applicant's election filed on January 5, 2004 wherein seborrheic keratosis was elected as the condition, and trypsin was elected as the hydrolase).

Claim Objections

Claims 1, 24, 30, and 34 are objected to because of the following informalities: Each of this claims recite "$\%^{w/v}$" which is improper notation. It is suggested that every instance of "$\%^{w/v}$" be replaced with "% w/v". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 40 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The terms "relatively short" and "relatively low" in claim 40 are relative terms which render the claim indefinite. It is unclear what durations of exposure are considered to be "relatively short" or what hydrolase concentrations are considered to be "relatively low." The terms are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Thus, claim 40 is rejected under 35 U.S.C. 112, second paragraph.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 34, 35, 37-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over SU 1685448.

SU 1685448 discloses treating seborrheic keratopapilomata (skin condition seborrheic keratosis) with a composition comprising trypsin as well as theophylline and dimexidum (dimethylsulfoxide – DMSO) (last paragraph, page 1 of English Translation of SU `448). Topical application of the disclosed composition of trypsin, theophylline, and DMSO to seborrheic keratopapilloma resulted in "a regression of swelling," which, following weeks of

treatment, eventually led to the disappearance of the swelling (last paragraph, page 3 through first paragraph, page 4 of English Translation of SU '448). Thus, the reference clearly taught the treatment of seborrheic keratosis by topical application of a composition **containing** the hydrolase trypsin, at a concentration selective for regulating depth of skin treatment, as well as regulating removal of the swelled layer.

SU '448 does not expressly disclose the concentration of hydrolase trypsin recited in parent claim 34. However, the selection of a specific suitable concentration, including that claimed, clearly would have been an obvious matter of optimization on the part of the artisan of ordinary skill in the art, as it depends on the amount of base used in the SU '448 composition (see last paragraph, page 3 of English Translation). A holding of obviousness is clearly required.

In the response filed on September 7, 2006, applicant requested clarification regarding the amendments. It is pointed out that unlike claims 1, 24, 26, 30, and 32, claims 34-35 and 37-40 do not recite "consisting essentially of," and instead, recite a composition "containing at least one hydrolase..." The amendment of transitional phrasing from "comprising" to "consisting essentially of" had not been made to claims 34-35 and 37-40 in the course of prosecution.

Claims 1-2, 4-5, 8-9, 24-25, 30-31, 34-35, 37-40 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over the disclosure of SU1685448 in view of Zaias (U.S. 5,411,741), Rawlings et al. (U.S. 5,665,366), and Burbach (Dermatologica 118: 379-391 (1959)).

As discussed above, SU 1685448 render claims 34, 35, and 37-40 obvious. However, SU 1685448 differs from the other claims in that SU 1685448 does not recite the application of a composition *consisting essentially* of the hydrolase trypsin.

Zaias, which discusses conventional carriers for skin treating compositions delivered to the epidermis (specifically depigmentation agents), teaches against the inclusion of DMSO as a carrier for compositions for treating the skin. At col. 3, lines 5-10, the Zaias patent states that DMSO causes extreme skin irritation, redness, itching and scaling. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to practice the method of treating seborrheic keratosis disclosed by SU1685448 by administering a composition containing trypsin but eliminating the DMSO. One of ordinary skill in the art would have been motivated to remove the DMSO since it is known to cause skin irritation. One of ordinary skill in the art would also still have a reasonable expectation of success by using only the trypsin as the active ingredient because of the disclosure of the other secondary references. Clearly, the artisan of ordinary skill in the art would have recognized that DMSO serves as a carrier of the SU '448 composition.

Additionally, Rawlings et al. teaches that the stratum corneum trypsin-like enzyme (SCTE) may be administered alone or in combination with suitable additional proteases such as trypsin to the skin in a vehicle. At col. 12, a composition of SCTE in ethanol, perfume, BHT and water is disclosed. No lanolin, theophylline or sunflower oil is necessary, yet this composition is disclosed as appropriate for the topical treatment of the skin for the disclosed purposes. Rawlings et al. discloses multiple formulations in multiple forms, all suitable for the administration of the SCTE and, if desired, trypsin to the skin for the treatment of conditions of the skin where the condition is characterized by hyperkeratinisation. At col. 9, lines 49-51, the amount of the composition and frequency of its application depends on the condition of the patient. It is noted that Rawlings et al. teaches dimethyl sulphoxide (DMSO) as an optional

alternative solvent and not a required component of the enzyme composition. See col. 3, lines 23-28.

Also, the disclosure of Burbach indicates the effect on human skin of proteases, and specifically trypsin, in varying amounts. The conclusion was that trypsin solutions, dependent upon concentration and period of application, were capable of breaking up the connection between the epidermis and the corium (dermis). The reference indicates at page 383 that crystalline trypsin would effect complete detachment of the epidermis after 1-2 hours after injection and disintegration of the epidermis after 3-4 hours after injection

Therefore, the selectivity of trypsin for the epidermal layer as a substrate was well known and the result of topical or injected application of trypsin to the epidermis was known and expected. Therefore the use of a composition consisting essentially of trypsin would have been obvious to one of ordinary skill in the art at the time the invention was made in order to effect a regulated removal of specific areas of the epidermis afflicted by seborrheic keratosis. Thus, a holding of obviousness is clearly required.

Claims 1, 2, 4, 8, 24, 30, 31, 34, 35, 37, 38, 39, and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klein et al. (US 4,226,854) or Fortney et al. (US 5,145,681).

Klein et al. discloses "a method for debridement of devitalized tissue from a mammalian host which comprises contacting said tissue with an amount of an enzyme product...which is effective to hydrolyze that portion of the devitalized tissue...and removing said devitalized tissue from the vital tissue, said enzyme product being a heat labile protein which is obtainable from bromelain" (claim 1). It is noted that materials which digest devitalized tissue while not

attacking viable tissue would make it possible to remove devitalized tissue without surgery, and these materials would serve as beneficial therapeutic agents "...in virtually all disease processes where topically devitalized tissue needs to be remove....such as decubitus ulcers, pressure necroses, incisional traumatic and pyogenic wounds, and ulcers secondary to peripheral vascular disease" (column 1, lines 23-30). Given that the removal of devitalized tissue is beneficial for the treatment of various diseases such as those listed above, Klein et al. clearly teaches a method for treating a patient having a condition affecting at least one layer of skin, and a method for targeting skin treatment of an affected area. The enzyme product of the Klein invention is considered to consist essentially of hydrolytic enzymes (hydrolases). Note that MPEP § 2111.03 clearly states that "[t]he transitional phrase 'consisting essentially of' limits the scope of a claim to the specified materials or steps 'and those that do not materially affect the basic and novel characteristic(s)' of the claimed invention." (Citations omitted, emphasis in original.) Moreover, MPEP § 2111.03 states that claims recited in "consisting essentially of" language should be construed as if recited in open "comprising" language, absent some evidence that the additional ingredients in the prior art process/product materially affect the basic and novel properties of the claimed invention:

> For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising." See, e.g., *PPG* [*Industries v. Guardian Industries*], 156 F.3d at 1355, 48 USPQ2d at 1355 ("PPG could have defined the scope of the phrase 'consisting essentially of' for purposes of its patent by making clear in its specification what it regarded as constituting a material change in the basic and novel characteristics of the invention."). See also *In re Janakirama-Rao*, 317 F.2d 951, 954, 137 USPQ 893, 895-96 (CCPA 1963).

Fortney et al. discloses "a method of removing necrotic tissue from a wound comprising contacting said wound with an effective amount for removing necrotic tissue of a protease..." (claim 14). It is noted that materials which digest devitalized tissue while not attacking viable tissue would make it possible to remove devitalized tissue without surgery, and these materials would serve as beneficial therapeutic agents "...in virtually all disease processes where topically devitalized tissue needs to be remove....such as burns, decubitus ulcers, pressure necroses, incisional traumatic and pyogenic wounds, and ulcers secondary to peripheral vascular disease" (column 1, lines 24-33). Given that the removal of devitalized tissue is beneficial for the treatment of various diseases such as those listed above, Fortney et al. clearly teaches a method for treating a patient having a condition affecting at least one layer of skin, and a method for targeting skin treatment of an affected area. The topically administered composition of the Fortney invention is considered to consist essentially of protease as the composition includes a topical carrier (column 2, lines 33-36) which clearly does not materially affect the basic and novel characteristics of the claimed invention. See the discussion above concerning MPEP § 2111.03.

Klein et al. and Fortney et al. differ from the claimed invention in that they do not teach the hydrolase concentration recited in instant claims 1, 24, 30, and 34. However, the selection of a specific suitable concentration, including that claimed, clearly would have been an obvious matter of optimization on the part of the artisan of ordinary skill in the art. A holding of obviousness is clearly required.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan E. Fernandez whose telephone number is (571) 272-3444. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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